

What is claimed is:

1. A crystallized complex of Beta-site APP Cleaving Enzyme (BACE) and SER-GLU-VAL-ASN-Sta-VAL-ALA-GLU-PHE.
2. The crystallized complex of Claim 1, wherein BACE has an N-terminal domain consisting of amino acid residues 58-207 shown in Figure 1, and a C-terminal domain consisting of amino acid residues 208-447 shown in Figure 1.
3. An active site of an APP binding protein or peptide comprising the relative structural coordinates according to Figure 1 of residues SER71, GLY72, LEU91, ASP93, GLY95, SER96, VAL130, PRO131, TYR132, THR133, GLN134, ILE171, ILE179, ILE187, ALA188, ARG189, PRO190, TRP258, TYR259, ASP284, LYS285, ASP289, GLY291, THR292, THR293, ASN294, ARG296 and ARG368, \pm a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 \AA .
4. The active site of Claim 3, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0 \AA .
5. The active site of Claim 3, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5 \AA .
6. An active site of an APP binding protein or peptide comprising the relative structural coordinates according to Figure 1 of residues LYS70, SER71, GLY72, GLN73, GLY74, TYR75, LEU91, VAL92, ASP93, THR94, GLY95, SER96, SER97, ASN98, TYR129, VAL130, PRO131, TYR132, THR133, GLN134, GLY135, LYS136, TRP137, LYS168, PHE169, PHE170, ILE171,

ASN172, SER174, TRP176, GLY178, ILE179, LEU180, GLY181, ALA183, TYR184, ALA185, GLU186, ILE187, ALA188, ARG189, PRO190, ASP191, ASP192, ARG256, TRP258, TYR259, TYR283, ASP284, LYS285, SER286, ILE287, VAL288, ASP289, SER290, GLY291, THR292, THR293, ASN294, LEU295, ARG296, GLY325, GLU326, ARG368, VAL370, LYS382, PHE383, ALA384, ILE385, SER386, GLN387, SER388, SER389, THR390, GLY391, THR392, VAL393, GLY395, ALA396 and ILE447, \pm a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 \AA .

7. The active site of Claim 6, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0 \AA .

8. The active site of Claim 6, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5 \AA .

9. A method for identifying an agent that interacts with an active site of Beta-site APP Cleaving Enzyme (BACE), comprising the steps of:

- (a) determining an active site of BACE from a three dimensional model of BACE using the relative structural coordinates of Figure 1, \pm a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 \AA ; and
- (b) performing computer fitting analysis to identify an agent which interacts with said active site.

10. The method of Claim 9, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0 \AA .

11. The method of Claim 9, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5 \AA .

12. A method for identifying an agent that interacts with an active site of an APP binding protein or peptide, comprising the steps of:

(a) generating a three dimensional model of an active site of an APP binding protein or peptide using the relative structural coordinates according to Figure 1 of residues SER71, GLY72, LEU91, ASP93, GLY95, SER96, VAL130, PRO131, TYR132, THR133, GLN134, ILE171, ILE179, ILE187, ALA188, ARG189, PRO190, TRP258, TYR259, ASP284, LYS285, ASP289, GLY291, THR292, THR293, ASN294, ARG296 and ARG368, \pm a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 \AA ; and

(b) designing an agent using the three dimensional model generated in step (a).

13. The method of Claim 12, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0 \AA .

14. The method of Claim 12, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5 \AA .

15. The method of Claim 12, wherein the agent is designed by performing computer fitting analysis of the agent with the three dimensional model generated in step (a).

16. The method of Claim 12, further comprising the steps of: (c) obtaining or synthesizing the agent so designed; and (d) contacting the agent with the APP binding protein or peptide in order to determine the effect the agent has on the APP binding protein or peptide.

17. The method of Claim 12, wherein the APP binding protein or peptide is BACE.

18. The method of Claim 17, wherein the agent is a potential inhibitor of binding between BACE and APP.

19. The method of Claim 18, further comprising the steps of:
(c) obtaining or synthesizing the agent so designed; and (d) contacting the agent with BACE in the presence of APP.

20. A method for identifying an agent that interacts with an active site of an APP binding protein or peptide, comprising the steps of:

(a) generating a three dimensional model of an active site of an APP binding protein or peptide using the relative structural coordinates according to Figure 1 of residues LYS70, SER71, GLY72, GLN73, GLY74, TYR75, LEU91, VAL92, ASP93, THR94, GLY95, SER96, SER97, ASN98, TYR129, VAL130, PRO131, TYR132, THR133, GLN134, GLY135, LYS136, TRP137, LYS168, PHE169, PHE170, ILE171, ASN172, SER174, TRP176, GLY178, ILE179, LEU180, GLY181, ALA183, TYR184, ALA185, GLU186, ILE187, ALA188, ARG189, PRO190, ASP191, ASP192, ARG256, TRP258, TYR259, TYR283, ASP284, LYS285, SER286, ILE287, VAL288, ASP289, SER290, GLY291, THR292, THR293, ASN294, LEU295, ARG296, GLY325, GLU326, ARG368, VAL370, LYS382, PHE383, ALA384, ILE385, SER386, GLN387, SER388, SER389, THR390, GLY391, THR392, VAL393, GLY395, ALA396 and ILE447, \pm a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 \AA ; and

(b) designing an agent using the three dimensional model generated in step (a).

21. The method of Claim 18, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0 \AA .

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22. The method of Claim 20, wherein the \pm a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5 Å.

23. The method of Claim 20, wherein the agent is designed by performing computer fitting analysis of the agent with the three dimensional model generated in step (a).

24. The method of Claim 20, further comprising the steps of:
(c) obtaining or synthesizing the agent so designed; and (d) contacting the agent with the APP binding protein or peptide in order to determine the effect the agent has on the APP binding protein or peptide.

25. The method of Claim 20, wherein the APP binding protein or peptide is BACE.

26. The method of Claim 25, wherein the agent is a potential inhibitor of binding between BACE and APP.

27. The method of Claim 26, further comprising the steps of:
(c) obtaining or synthesizing the agent so designed; and (d) contacting the agent with BACE in the presence of APP.

28. An agent identified by the method of Claim 9.

29. An agent identified by the method of Claim 12.

30. An agent identified by the method of Claim 20.